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June 29, 2006

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Sir:

Re: United States Patent Application No. 10/757,937
Filed: January 16, 2004
Title: N-Time-Gate Data-Type for TPSF-Based Optical Imaging
Inventor: David Jonathan HALL
Assignee: ART, Advanced Research Technologies, Inc.
Our File: 15186-23US

Enclosed herewith for filing against the above-identified application, is the required certified copies of the priority applications in this matter, i.e. International Patent Application Nos. PCT/CA02/01067 filed July 16, 2002 and PCT/CA03/00047 filed January 22, 2003.

Respectfully submitted,

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Encls.



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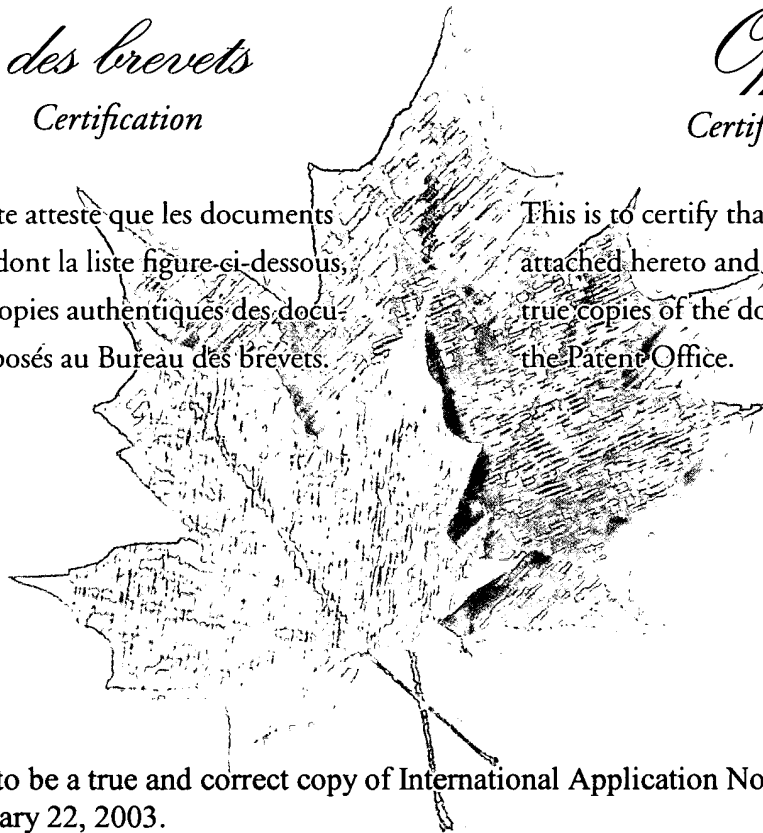
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N-Time-Gate Data-Type for TPSF-Based Optical Imaging

TECHNICAL FIELD

This invention relates to the field of temporal point
5 spread function (TPSF) based imaging in which objects which
diffuse light, such as some human body tissues, are imaged
using signals resulting from the injection of light into
the object and detection of the diffusion of the light in
the object at a number of positions while gathering TPSF-
10 based data to obtain information beyond simple attenuation
such as scattering and absorption. More particularly, the
present invention relates to a specific data-type, N-time-
gate, which can be obtained from TPSF-based data.

BACKGROUND OF THE INVENTION

15 Time-domain optical medical imaging shows great promise as
a technique for imaging breast tissue, as well as the brain
and other body parts. The principle of the technique lies
in the analysis of the temporal point spread function
(TPSF) of an injected pulse of light which is diffused in
20 an object of interest (OOI), and in the extraction of
information from the TPSF to construct a medically useful
image. The (complete) TPSF is defined as the light
intensity of a given wavelength presented as a function of
time t ($t_0 \leq t \leq \infty$) that can be observed at a given spatial
25 location after a very short pulse of light produced at
another spatial location at the time t_0 .

Specific types of data extracted from the TPSF are known as
'Data-types'. For example, 'early time-gated attenuation'
is a Data-type that can be extracted from the TPSF which
30 improves the image spatial resolution over continuous wave

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methods. However, it is unclear whether such improvements in image spatial resolution are adequate for diagnosing certain diseases, such as breast cancer, based on morphology.

- 5 An alternative approach is to use the TPSF to decouple the light attenuation into absorption and scattering components. This extra information, which generally cannot be obtained with continuous wave methods, may be clinically useful. In order to achieve this it is customary to extract
- 10 appropriate Data-types from the TPSF. Researchers, in the time-domain field, have looked at data-types such as the meantime and higher moments of the TPSF (Arridge, 1999). Whilst data-types for optical data acquired in the frequency domain have included phase-shift and amplitude.
- 15 There are several techniques for measuring the TPSF arising from a light pulse that has traveled through an OOI such as breast tissue. Certainly the most information one can acquire is by measuring a complete TPSF. This information can also be acquired in the frequency domain, although
- 20 current hardware limitations mean that time-domain hardware is capable of acquiring information over a larger bandwidth than its frequency domain counterpart.

However, acquiring a practical approximation $f(t), t \in [a, b]$ to the complete TPSF, such that $\int_a^b f(t) dt \approx \int_a^b f(t) dt$, has implications

25 in terms of long acquisition times for clinical systems, and possibly unacceptably long data-processing for image reconstruction algorithms.

It would therefore be desirable to provide methods overcoming the limitations of the prior art.

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SUMMARY OF THE INVENTION

For the purpose of image construction, the entire TPSF derived from a pulse of light can be used. The streak camera has commonly been used for this purpose. However, the
5 detection surface of a streak camera may be limited. Time-gated cameras such as intensified charge coupled device (ICCD) typically have greater detection surface areas but acquisition of complete TPSFs using such camera may be time consuming.

10 It is therefore an object of the present invention to provide a method and apparatus for TPSF-based imaging of an object in which acquisition times are reduced while still extracting a sufficient amount of desired information from the TPSF of a collected optical signal to be used in
15 producing an optical image.

According to a broad aspect of the invention this objective is achieved by detecting selected intervals, or N-time-gates, of a TPSF. The detection of the selected time-gates is effected using time-gated detection techniques and
20 cameras.

In a further aspect of the invention, the acquisition time is substantially reduced by simultaneously detecting selected time gates of a TPSF.

Thus in one aspect of the present invention there is
25 provided a method for simultaneously detecting N-time-gates Data-type of a TPSF of a collected optical signal, the method comprising pulsing the object with a light pulse delivered at one or more injection ports, collecting a plurality of optical signals based TPSF's at collection
30 ports, introducing delays in propagation of the optical

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signals to produce staggered TPSF's and simultaneously detecting selected time-gates.

In an embodiment of the invention the delays in the propagation of the optical signals are provided by using
5 optical fibers of different lengths to collect the optical signals.

BRIEF DESCRIPTION OF THE DRAWINGS

Further features and advantages of the present invention will become apparent from the following detailed
10 description, taken in combination with the appended drawings, in which:

Fig. 1 is a diagram showing an embodiment of the system used to generate a pulse of light and to produce a TPSF after injection of the light in an object;

15 Fig. 2 is a graphical representation of a TPSF showing arbitrarily defined time-gates;

Fig. 3 is an example of a system that can be used to construct an optical image according to methods of the present invention;

20 Fig. 4 is a schematic representation of an embodiment of the system used to simultaneously detect two or more time-gates;

Fig. 5 is a graphical representation of three staggered TPSF's;

25 Fig. 6A is a plot of intensity over time in arbitrary units (i.e. a TPSF) along with a first derivative; and

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Fig. 6B is a plot of the first derivative of Fig. 6A along with a second derivative.

It will be noted that throughout the appended drawings, like features are identified by like reference numerals.

5 DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

In accordance with the present invention, there is provided a method and apparatus using a N-time-gate Data-Type for TPSF-based optical imaging.

Figure 1 schematically represents the events giving rise to
10 a TPSF. A pulse of light 2 is generated at a source 10 and injected in an OOI 4 at injection port 14. The OOI may be a body part such as a breast but it will be appreciated that the method and apparatus described herein can be applied to any suitable object. The light interacts with the medium by
15 being absorbed and/or scattered and exits the OOI with an attenuated intensity. The exiting attenuated light can be collected at collection port 18 as a function of time to produce the TPSF 6. The shape of the TPSF depends on the type of interactions that occurred between the light and
20 the medium. Images (maps of optical properties) may be constructed by extracting appropriate Data-types from the TPSF and by inputting them to an appropriate image reconstruction algorithm, i.e. one which forward models the data and solves the appropriate inverse problem.

25 In one embodiment, the present invention provides a method for detecting only selected intervals of a TPSF. In Figure 2 it can be seen that a TPSF can be subdivided in n arbitrary intervals 8 which will be referred to as time-gates (tg) hereinafter. The time-gate is defined as an
30 interval $[a, b) \subset [t_0, \infty)$, where a and b are predefined constants.

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Therefore one can consider a complete TPSF as being constructed from many individual time-gate signals. The actual time points that define the beginning and the end of a time-gate are preferably determined relative to the time, t_0 , at which the light pulse is injected into the object. By detecting the signal of sequential time-gates using time gated detection techniques and cameras such as, but not limited to, a time-gated intensified charge coupled device (ICCD), it is possible to acquire the complete TPSF. However, acquisition of a complete TPSF in this manner requires long acquisition times which will be proportional to the number of time-gates acquired. In one aspect of the present invention the image may be constructed by acquiring only certain time-gates. As a result the acquisition time is greatly reduced. Overlapping time-gates can be allowed if the forward model is capable of taking this into account.

The selection of the time-gates relative to t_0 that will be used to construct an image may be based on the characteristics of the object such as the thickness and the anticipated optical properties. In the absence of prior knowledge about the anticipated optical properties of the object, a practical approximation to the complete TPSF could be obtained and be used for future selection of the time-gates.

In a preferred embodiment certain specific time gates or time points (infinitely small time gates) of the TPSF at which TD data will be acquired can be selected based on the following approach:

Based on the physics of diffuse light propagation, it can be assumed that a noiseless TPSF is a continuous and

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infinitely differentiable function defined on R^+ . Critical points of a function can be identified via zeros of this function's derivative. Due to the fact that a TPSF has a characteristic shape (see 6 Figure 1), the i -th derivative will yield a set of points where it became zero, which corresponds to extreme values of the underlying function. The first subset $s_1 = \{s_{1,1}\}$ corresponding to the 1st derivative describes the unique TPSF maximum. The second subset $s_2 = \{s_{2,1}; s_{2,2}\}$ corresponding to the 2nd derivative reveals two points where the curvature directionality changed. Derivatives of the higher order yield information on more subtle TPSF shape features. The subset s_i corresponding to the i -th derivative can be defined as $s_i = \{s_{i,1}; \dots; s_{i,j}\}$.

Given a TPSF $f(t)$ represented with a set of M values ($M \gg n$), e.g. $f = \{f(t_1), f(t_2), \dots, f(t_M)\}$, $t_1 \geq a$, $t_M \leq b$, one can perform recursive numerical "differentiation" of the TPSF and of its' resulting "derivatives" by computing the quotient:

$$Q_i = \frac{f(t_{i+1}) - f(t_{i-1})}{t_{i+1} - t_{i-1}},$$

which would approximate the value of the derivative $f'(t_i)$.

- 20 When plotted, characteristic sequence of functions will emerge as shown in Figures 6A and 6B. One observes that in this example $s_1 = \{31.5\}$, $s_2 = \{20.5; 40.5\}$, $s_3 = \{14.5; 25.5; 48.5\}$, the values being the time point indices rather than absolute time.
- 25 In order to obtain an adequate TPSF representation with n points (or time gates), one would want to reflect the TPSF

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shape as fully as possible. The sequence $\{s_1; s_2; \dots\}$ allows for identification of the most relevant points in the order of diminishing significance as the subset number increases. Note that elements within a given subset s_i have equal
5 significance with a noiseless TPSF. However, elements of s_i may be ordered by assigning higher priority to elements that have higher $\max_{k \in \{1, \dots, K\}} |s_{i,j} - s_{k,j}|$ in order to minimize the correlation of experimental errors.

One can consider s_i the midpoints of a set of time-gates s'_i ,
10 i.e. $s'_i = \{[s_{i,1} - 0.5r_{i,1}, s_{i,1} + 0.5r_{i,1}), \dots, [s_{i,n} - 0.5r_{i,n}, s_{i,n} + 0.5r_{i,n})\}$, where $r_{i,j}$ is the width of a respective time gate.

The procedure outlined above can yield $S' = \{s'_1; s'_2; \dots\}$, $i=1, \dots, K$ for a given TPSF having index i . In order to reflect the most relevant features of a set of K TPSFs, one must arrive to
15 $S_1 = s'_1 \cup s'_2 \cup \dots \cup s'_K$ first, to $S_2 = s'_1 \cup s'_2 \cup \dots \cup s'_K$ second and so on. The set $\{S_1; S_2; \dots\}$ provides a sequence whose n starting elements should be used to represent the set of TPSFs in an optimal manner.

As mentioned above, s'_m might be replaced with a set of
20 intervals in order to analyze time-gates instead of time points.

In a preferred embodiment of the invention the steps to select the appropriate time gates are as follows:

- Acquire practical approximations to the complete TPSFs
25 for all source-detector pairs that are capable of functioning simultaneously. At least one typical source position through the bulk medium should be used. The

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robustness of the subsequent analysis increases, as more typical source positions are included.

- Approximate all measured TPSFs either based on a relatively simple model of photon propagation, e.g. assuming that propagation took place in a homogeneous medium, or interpolate the measured TPSFs to ensure the continuity and differentiability of the result.
- Perform analysis yielding the set $\{S_1, S_2, \dots\}$ as described above in order to determine the optimal n time-gates.
- 10 - Acquire data with the determined n time-gates. n is an input parameter. In practice it can be determined via estimation of the resulting data set size that can be utilized to reconstruct images within a desired time frame.

- Temporal resolution r_0 , i.e. the minimal distance between t_i and t_{i+1} that yields virtually "uncorrelated" values $f(t_i)$ and $f(t_{i+1})$; is determined by the limitations of the data acquisition hardware and is, therefore, an input parameter. It is preferable to perform initial data acquisition with time-gate width and time steps of not more than $0.5 \times r_0$.
- 15 and t_{i+1} that yields virtually "uncorrelated" values $f(t_i)$ and $f(t_{i+1})$; is determined by the limitations of the data acquisition hardware and is, therefore, an input parameter. It is preferable to perform initial data acquisition with time-gate width and time steps of not more than $0.5 \times r_0$.
 - 20 Eventual width $r_i \geq r_0$ of the time-gate having index i is automatically chosen to ensure capturing the most relevant TPSF features revealed by the analysis.

- The above described method for selecting time gates may be used in the context of a broader process for selecting appropriate time-gates when imaging a particular object. In one embodiment this broader process may comprise the use of banks of TPSF's obtained from a plurality of objects having given recorded characteristics and for which the derivative method described above has been applied to select
- 25 appropriate time-gates when imaging a particular object. In one embodiment this broader process may comprise the use of banks of TPSF's obtained from a plurality of objects having given recorded characteristics and for which the derivative method described above has been applied to select

- 10 -

appropriate time-gates. Thus, the selection of appropriate time-gates for a new object being imaged may then be made by matching certain predetermined characteristics of the object with those recorded in the data banks. When a "good" match has been found the time-gates that have been identified for the corresponding object in the data bank are used to acquire the TPSF of the object being imaged. For example, in the case of breast imaging, TPSF's can be acquired from a plurality of patients having different characteristics that can be recorded such as age, breast density, disease state etc. The derivative method is then applied to these TPSF's to select appropriate time-gates and the identity of the time-gates are associated with each patient. When it is desired to image the breast of a new patient the appropriate time-gates may be selected by simply matching the characteristics of this patient with those in the data bank thereby effecting the selection of the time-gates. It will be appreciated that the characteristics used in the data bank maybe chosen to reflect their relevancy to optical imaging.

An embodiment of the system that can be used to perform the data acquisition using the method of the present invention is schematically represented in Figure 3. The pulsed light source 10 has an output optically coupled via a switch 12 to one or a plurality of injection ports 14 of a support. The injections port are preferably positioned at a number of fixed positions over the imaging area although the injection ports may alternatively be moveable over the body surface, provided that the body part 16 being imaged is immobilized. As is known in the art the injection and collection ports may directly contact the body or a coupling medium may be used between the body and the

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injection/collection ports. In Figure 3, the collection ports 18 and support are arranged in transmission mode for breast imaging. However, it is also possible to have an injection ports/object/collection ports geometry such that the collection ports are on the same surface as the injection ports. The light source may be a polychromatic source or a monochromatic source such as a laser. The pulses preferably have a duration of about 1 to 100 picoseconds and an average power of 100 mW.

10 The collected optical signals may be communicated by one or more waveguides 20 such as 400/440 micron graded index multimode optical fibers to one or more detection positions of a time gated detector 22 such as a gated ICCD camera, for example a PicoStar™ camera by LaVision.

15 A large number of pulses may be injected and their corresponding camera signals detected and processed by imaging computer 24 to determine the value of at least one time gate and, in the case of simultaneous detection, two or more selected time gates of a TPSF. Such data are
20 gathered for a sufficiently large number of detecting port positions to ensure robust reconstruction of an image of the object. The resulting image can be displayed on a monitor 26 or a hard copy can be obtained at 28.

It will be appreciated that the relative positions of the
25 injectors and detectors may be modified as needed to optimize the quality of the image. Thus different geometries of the injection ports/collection ports/object assembly may be used, for example by placing collection ports either proximally or distally or a combination of
30 both, depending on several factors such as, the thickness of the object, the nature of the medium comprising the

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object. The value for each pixel or voxel of an image generated from the data collected according to the present invention will benefit from a plurality of source detector locations with respect to the position of the pixel or voxel, as well as a plurality of time-gates.

In an aspect of the present invention the acquisition time can be further reduced by simultaneously detecting a desired number of time-gates of one or more TPSF's. This can be achieved by collecting the light signal exiting from the COI at several (m) locations. Temporal delays are then introduced in the propagation of these optical signals such that the m TPSF's reach the time-gated detector in a staggered manner. Therefore, using a time-gated camera, it is possible to simultaneously detect m different time-gates of the TPSF's.

This embodiment of the invention will be better understood with reference to Figures 4 and 5. In Figure 4 a schematic diagram of a possible arrangement of a system used to simultaneously detect m time gates is depicted. In this embodiment optical fibers 30 are used to collect and channel the light exiting the COI 4 to a time-gated detector 32. The fibers are of different lengths and therefore the time required for the optical signal to travel from the collecting point to the detection point at the detector is different for each fiber thus introducing delays in the propagation of the optical signal. Each fiber, or bundle of fibers, is coupled to a different detection position 34 at the detector. Consequently, the time required for a particular time gate, t_g , to reach the detection position in the detector will depend on the length of the fiber through which it is propagated. Figure 5 is a graphic representation of three staggered TPSF's

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propagated by three different optical fibers F1, F2, and F3 having different lengths with length of F1 > length of F2 > length of F3. It can be appreciated that a given time-gate, say tg3, reaches the detector at a different time depending on whether it is propagated by F1, F2 or F3. Now if the detector is time-gated to detect only the signal during the interval defined by t1 and t2, different time-gates will be detected for each fiber. In our example tg3, tg5, and tg7 are simultaneously detected. It can be seen that the number of time gates that can be detected simultaneously is equal to the number of fibers. The fibers can be bundled within a defined area of a given detector and provide the desired time-gates simultaneously with one 'snapshot' of the time-gated camera. This leads to a decrease in the acquisition time by a factor of approximately n compared to serially acquired time-gates.

It will be appreciated that the length of the fibers can be selected to detect the desired time gates (or the desired sections of the TPSF). To refer to our example, if one wanted to simultaneously detect tg7, tg5 and tg1, the length of F1 could be increased accordingly. However, it will also be appreciated that the simultaneous detection of the desired time-gates can be effected by directing each fiber to a different detector and by adjusting the time gate of each detector so as to detect one of the desired time gate. Typically, an increase of 11 cm in fiber length will induce a time delay of about 500 ps.

The delays in the propagation of the optical signals may also be introduced by using variable delay optical waveguides that are well known in the art.

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It will be appreciated that the signal to noise ratio (SNR) may limit the number of fibers and thus the number of time gates that can be simultaneously detected. In practice, it is a decision between how many detector positions are
5 required, the number of time-gates simultaneously required and the total number of fibers which can be packed onto the gated camera. Referring back to Figure 4, it will be further appreciated that if the fibers or the fiber bundles
35 are sufficiently close together, the TPSF's may be
10 substantially identical.

The embodiment(s) of the invention described above is(are) intended to be exemplary only. The scope of the invention is therefore intended to be limited solely by the scope of the appended claims.